SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name: Iliac Stent

Device Trade Name: IntraStent® DoubleStrut™ Stent

Applicant's Name and Address: **ev3** Inc.
4600 Nathan Lane North
Plymouth, MN 55442

Premarket Approval (PMA) Application Number: P030045

Date of Panel Recommendation: N/A

Date of Notice of Approval to Applicant: June 8, 2004

II. Indications for Use

The IntraStent® DoubleStrut™ Stent is indicated for improving luminal diameter in patients with symptomatic atherosclerotic disease of the common and/or external iliac arteries up to 100 mm in length, with a reference vessel diameter of 5 to 10 mm.

III. Contraindications

There are no contraindications known at this time based on the clinical data.

IV. Warnings and Precautions

The warnings and precautions can be found in the labeling for the IntraStent DoubleStrut stent.

V. Device Description

The **ev3** IntraStent DoubleStrut stent is a balloon expandable slotted tubular stent, made from a 316 L stainless steel tube. The stent is electropolished and incorporates a microtextured surface at each end on the inner surface. The microtextured surface enhances the "grip" of the crimped stent on the balloon. The stent is unmounted and is hand crimped by the user onto a commercially available percutaneous transluminal angioplasty (PTA) balloon catheter prior to use.

The stent design utilizes a unique cell shape and incorporates paired elements throughout the center section of the stent. The paired elements maintain a slight separation (essentially remain parallel to each other) throughout the stent expansion range. Figure 1 presents a flat representation of the unexpanded stent design.

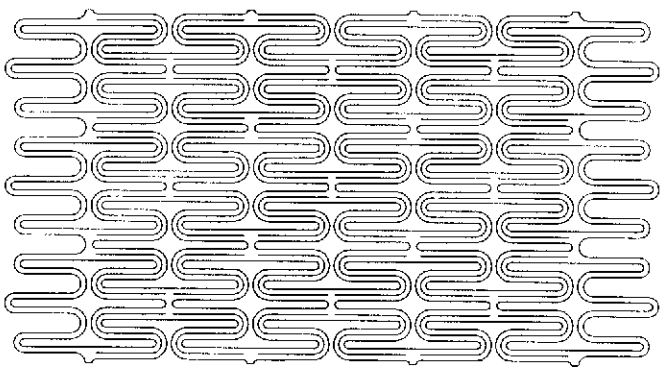

Figure 1. **ev3** IntraStent DoubleStrut stent – flat representation.

VI. Alternative Practices and Procedures

Alternative procedures to treat atherosclerotic disease of the iliac arteries include percutaneous transluminal angioplasty (PTA), surgical procedures, and other stents for which there is an approved PMA.

VII. Marketing History

The IntraStent DoubleStrut stent has been marketed for peripheral vascular use in the following major countries: Australia, Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Ireland, Italy, Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, and United Kingdom. The IntraStent DoubleStrut stent has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

VIII. Adverse Effects of the Device on Health

A. Observed Adverse Events

A total of 228 patients were enrolled in the multicenter, randomized study comparing the IntraStent DoubleStrut stent to the Schneider WALLSTENT® Endoprosthesis and the Cordis Palmaz® stent (control stents). Patients with a suboptimal PTA result during the treatment of a lesion in the common and/or external iliac artery were randomized to either the InstraStent DoubleStrut stent (N=115) or the control stents (N=113).

Table 1 (Evaluable) and Table 2 (Intent-to-Treat) below summarize major adverse events reported in both treatment groups to 9 months. There have been 17 deaths reported. One control group (Palmaz stent) patient died within the first 30 days of an undetermined cause. An additional nine control group patients (eight Palmaz and one Wallstent stents) died during follow-up (511, 529, 551, 599, 617, 722, 1032, 1277, 1290 days post-procedure); two of myocardial infarction (MI), three of cancer, one of cardiopulmonary arrest, one of cardiogenic shock, one of congestive heart failure (CHF) and one undetermined. Seven treatment group patients died during follow-up (201, 331, 391, 517, 542, 719, 1183 days post-procedure); one of MI, three of cancer, one of chronic obstructive pulmonary disease (COPD) exacerbation, one of cerebro-vascular accident (CVA) and one of sepsis.

Table 1. Major Observed Adverse Events (Evaluable)

Description of Event	IntraStent DoubleStrut Stent	Control Stents	Difference (95% CI)	P-Value
Complications ≤ 30 days				
Total Complications < 30 Days	2.7% (3/113)	8.9% (10/112)	6.3% [0.2%, 12.3%]	0.04
MAIE	0.0% (0/113)	2.7% (3/112)	2.7% [-0.3%, 5.7%]	0.08
Death within 30 Days	0.0% (0/113)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.32
MI (in hospital)	0.0% (0/113)	0.0% (0/112)	0.0% [0.0%, 0.0%]	.
Amputation of Target Limb	0.0% (0/113)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.32
Target vessel revascularization	0.0% (0/113)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.32
Stent Thrombosis	0.0% (0/113)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.32
Major bleeding complication	0.9% (1/113)	3.6% (4/112)	2.7% [-1.2%, 6.5%]	0.17
Major vascular complication	0.9% (1/113)	1.8% (2/112)	0.9% [-2.1%, 3.9%]	0.56
Renal Insufficiency	0.0% (0/113)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.32
Dissection	0.9% (1/113)	2.7% (3/112)	1.8% [-1.7%, 5.2%]	0.31
Stroke	0.9% (1/113)	0.0% (0/112)	-0.9% [-2.6%, 0.8%]	0.32
MI	0.0% (0/113)	0.0% (0/112)	0.0% [0.0%, 0.0%]	.
Complications > 30 days (to 9 Months)				
Total Complications > 30 Days	6.6% (7/106)	5.9% (6/102)	-0.7% [-7.3%, 5.9%]	0.83
MAIE	3.8% (4/106)	2.0% (2/102)	-1.8% [-6.3%, 2.7%]	0.43
Death within 30 Days	0.0% (0/113)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.32
MI (in hospital)	0.0% (0/106)	0.0% (0/102)	0.0% [0.0%, 0.0%]	.
Amputation of Target Limb	0.9% (1/106)	0.0% (0/102)	-0.9% [-2.8%, 0.9%]	0.32
Target vessel revascularization	4.7% (5/106)	2.9% (3/102)	-1.8% [-7.0%, 3.4%]	0.50
Death	0.9% (1/106)	0.0% (0/102)	-0.9% [-2.8%, 0.9%]	0.32
Stent Thrombosis	0.0% (0/106)	1.0% (1/102)	1.0% [-0.9%, 2.9%]	0.32
Major bleeding complication	0.9% (1/106)	1.0% (1/102)	0.0% [-2.6%, 2.7%]	0.98
Major vascular complication	0.0% (0/106)	0.0% (0/102)	0.0% [0.0%, 0.0%]	.
Renal Insufficiency	0.0% (0/106)	0.0% (0/102)	0.0% [0.0%, 0.0%]	.
Dissection	0.0% (0/106)	0.0% (0/102)	0.0% [0.0%, 0.0%]	.
Stroke	0.0% (0/106)	0.0% (0/102)	0.0% [0.0%, 0.0%]	.
MI	0.0% (0/106)	1.0% (1/102)	1.0% [-0.9%, 2.9%]	0.32
Cumulative Complications (to 9 Months)				
Total Complications - Combined	9.4% (10/106)	15.7% (16/102)	6.3% [-2.7%, 15.2%]	0.18
MAIE	3.8% (4/106)	4.9% (5/102)	1.1% [-4.4%, 6.7%]	0.69
Death within 30 Days	0.0% (0/113)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.32
MI (in hospital)	0.0% (0/106)	0.0% (0/102)	0.0% [0.0%, 0.0%]	.
Amputation of Target Limb	0.9% (1/106)	1.0% (1/102)	0.0% [-2.6%, 2.7%]	0.98
Target vessel revascularization	4.7% (5/106)	3.9% (4/102)	-0.8% [-6.3%, 4.7%]	0.78
Death	0.9% (1/106)	1.0% (1/102)	0.0% [-2.6%, 2.7%]	0.98
Stent Thrombosis	0.0% (0/106)	2.0% (2/102)	2.0% [-0.7%, 4.7%]	0.16
Major bleeding complication	1.9% (2/106)	4.9% (5/102)	3.0% [-1.9%, 7.9%]	0.23
Major vascular complication	0.9% (1/106)	2.0% (2/102)	1.0% [-2.2%, 4.3%]	0.54

Description of Event	IntraStent DoubleStrut Stent	Control Stents	Difference (95% CI)	P-Value
Renal Insufficiency	0.0% (0/106)	1.0% (1/102)	1.0% [-0.9%, 2.9%]	0.32
Dissection	0.9% (1/106)	2.9% (3/102)	2.0% [-1.8%, 5.8%]	0.30
Stroke	0.9% (1/106)	0.0% (0/102)	-0.9% [2.9%, -0.9%]	0.32
MI	0.0% (0/106)	1.0% (1/102)	1.0% [-0.9%, 2.9%]	0.32

Subjects were counted once for multiple occurrences of an adverse event
MAIE (Major Adverse Ischemic Event) = Any death within 30 days, MI (in-hospital), amputation of target limb or target vessel revascularization (TVR).
Major Complication = Includes death, stroke, bleeding requiring transfusion, myocardial infarction, embolism, or any complication that is procedure or device related which requires a surgical procedure, interventional procedure or extended hospital stay.
Difference = Control – Treatment; SE=sqrt(p1*q1/n1+p2*q2/n2) CI=Diff±1.96*SE

Table 2. Major Observed Adverse Events (Intent-to-Treat)

Description of Event	IntraStent DoubleStrut Stent (n=115)	Control Stents (n=113)	Difference (95% CI)	P-Value
Complications ≤ 30 days				
Total complications ≤ 30 days	2.6% (3/115)	8.8% (10/113)	6.2% [0.3%, 12.2%]	0.04
MAIE	0.0% (0/115)	2.7% (3/113)	2.7% [-0.3%, 5.6%]	0.08
Death within 30 days	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
MI (in-hospital)	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
Amputation of target limb	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
Target vessel revascularization	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
Stent thrombosis	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
Major bleeding complication	0.9% (1/115)	3.5% (4/113)	2.7% [-1.1%, 6.5%]	0.17
Major vascular complication	0.9% (1/115)	1.8% (2/113)	0.9% [-2.1%, 3.9%]	0.55
Renal insufficiency	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
Dissection	0.9% (1/115)	2.7% (3/113)	1.8% [-1.6%, 5.2%]	0.31
Stroke	0.9% (1/115)	0.0% (0/113)	-0.9% [-2.6%, 0.8%]	0.32
MI	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
Complications > 30 days (to 9 Months)				
Total complications > 30 days	6.1% (7/115)	5.3% (6/113)	-0.8% [-6.8%, 5.2%]	0.80
MAIE	3.5% (4/115)	1.8% (2/113)	-1.7% [-6.9%, 2.4%]	0.42
Death within 30 days	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
MI (in-hospital)	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
Amputation of target limb	0.9% (1/115)	0.0% (0/113)	-0.9% [-2.6%, 0.8%]	0.32
Target vessel revascularization	4.3% (5/115)	2.7% (3/113)	-1.7% [-6.5%, 3.1%]	0.48
Death	0.9% (1/115)	0.0% (0/113)	-0.9% [-2.6%, 0.8%]	0.32
Stent thrombosis	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
Major bleeding complication	0.9% (1/115)	0.9% (1/113)	-0.0% [-2.4%, 2.4%]	0.99
Major vascular complication	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
Renal insufficiency	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
Dissection	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
Stroke	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
MI	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
Cumulative Complications (to 9 Months)				
All combined	8.7% (10/115)	14.2% (16/113)	5.5% [-2.8%, 13.7%]	0.20
MAIE	4.3% (5/115)	4.4% (5/113)	0.1% [-5.2%, 5.4%]	0.98
Death within 30 days	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
MI (in-hospital)	0.0% (0/115)	0.0% (0/113)	0.0% [0.0%, 0.0%]	--
Amputation of target limb	0.9% (1/115)	0.9% (1/113)	0.0% [-2.4%, 2.4%]	0.99
Target vessel revascularization	4.3% (5/115)	3.5% (4/113)	-0.8% [-5.9%, 4.2%]	0.75
Death	0.9% (1/115)	0.9% (1/113)	-0.0% [-2.4%, 2.4%]	0.99
Stent thrombosis	0.0% (0/115)	1.8% (2/113)	1.8% [-0.7%, 4.2%]	0.15
Major bleeding complication	1.7% (2/115)	4.4% (5/113)	2.7% [-1.8%, 7.2%]	0.24
Major vascular complication	0.9% (1/115)	1.8% (2/113)	0.9% [-2.1%, 3.9%]	0.55
Renal insufficiency	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31
Dissection	0.9% (1/115)	2.7% (3/113)	1.8% [-1.6%, 5.2%]	0.31
Stroke	0.9% (1/115)	0.0% (0/113)	-0.9% [-2.6%, 0.8%]	0.32
MI	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31

Subjects were counted once for multiple occurrences of an adverse event
MAIE (Major Adverse Ischemic Event) = Any death within 30 days, MI (in-hospital), amputation of target limb or target vessel revascularization (TVR).
Major Complication = Includes death, stroke, bleeding requiring transfusion, myocardial infarction, embolism, or any complication that is procedure or device related which requires a surgical procedure, interventional procedure or extended hospital stay.
Difference = Control – Treatment; SE=sqrt(p1*q1/n1+p2*q2/n2) CI=Diff±1.96*SE

B. Potential Adverse Events

Adverse events that may be associated with implantation of a stent in the iliac arteries (in addition to those listed in Table 1) include:

- Allergic/anaphylactoid reaction
- Aneurysm
- Angina/coronary ischemia
- Arterial occlusion/thrombus, at puncture site or remote
- Arterial occlusion/restenosis of the treated vessel
- Arteriovenous fistula
- Arrhythmia
- Death related/unrelated to procedure
- Embolization, arterial or other
- Hematoma
- Hypotension/hypertension
- Intimal injury/dissection
- Ischemia/infarction of tissue/organ
- Local infection
- Malposition (failure to deliver the stent to intended site)
- Migration
- Pulmonary embolism
- Pseudoaneurysm
- Renal failure
- Septicemia/bacterimia
- Stent fever
- Vasospasm
- Venous occlusion/thrombus at puncture site or remote

C. Observed Device Malfunctions

There were no delivery failures or stent malfunctions observed with the IntraStent DoubleStrut stent or control stents.

IX. Summary of Non-Clinical Laboratory Studies

A. Biocompatibility

The IntraStent DoubleStrut stent is comprised solely of 316L stainless steel that meets the requirements of ASTM F138 and F139. Because 316L stainless steel used in the IntraStent DoubleStrut stent meets this ASTM standard and has been used throughout the medical device industry as an implant, it is accepted that the biocompatibility requirements of the material per ISO 10993-1, "Biological Evaluation of Medical Devices Part 1: Evaluation of Testing" and FDA's blue book memorandum dated May 1, 1995 have been demonstrated. The following biocompatibility tests were performed on devices that have undergone all of the manufacturing steps, including sterilization: cytotoxicity, hemolysis, material mediated pyrogenicity, acute systemic toxicity, intracutaneous reactivity, sensitization, and ongoing pyrogen (endotoxin) testing. The results demonstrated that the materials are non-toxic and non-pyrogenic.

B. Bench Testing and Calculations

Magnetic Resonance Imaging (MRI) Compatibility
The IntraStent DoubleStrut stent has not been tested for safety in the MR environment. Therefore, MRI scans should not be performed on patients post-implantation until the stent has completely endothelialized to minimize the potential for migration. For a conventional uncoated 316L stainless steel stent, this period is usually considered to be 8 weeks. This device has not been evaluated for heating in the MR environment.

Other Bench Testing
Information on bench testing of the IntraStent DoubleStrut stent is summarized in Table 3 below. In all cases, results demonstrated compliance with the established specifications after being processed through the manufacturing steps.

Table 3. Preclinical Testing Summary for IntraStent DoubleStrut Stent

Test	Objective/Method	Acceptance Criteria
Material Analysis/ Mechanical Properties	To verify that materials meet the minimum requirements of ASTM F138 and ASTM F139.	Must meet the minimum specifications of ASTM F138/F139.
Metallurgical/Material Analysis	Inspect raw, in-process and finished 316L for differences via light microscopy and scanning electron microscopy.	Must not be visible differences from a metallurgical standpoint between test samples.
Corrosion Testing	To verify that no rust staining, discoloration or pitting is visually observed.	No rust, discoloration or pitting evident when observed under 40X magnification.
Stent Crimping/Mounting	Verify that the stent has a large enough inside diameter to fit over the balloon and that the stent can be fully compressed onto the balloon by applying direct radial pressure with both thumbs and index fingers.	The stent must fit onto and be able to be firmly compressed onto the balloon along its entire length.
Crossing Profile	Measure the diameter of the stent at three points while crimped onto a balloon.	The stent, when mounted on the balloon catheter, must be small enough to be compatible with a 7Fr or smaller sheath.

Test	Objective/Method	Acceptance Criteria
Stent Retention/Bend Radius Test	Determine whether a crimped stent can be passed through an introducer sheath without dislodging the stent from the balloon by advancing the system over a 0.035" guidewire and passing it through an introducer sheath which is formed around a one inch radius.	2mm or less movement of the stent on the balloon and the stent must pass through the sheath with minimum resistance.
Stent Retention Forces	Determine the force in grams required to move the stent on the balloon. Stent is crimped with suture tied in two locations. Tensile testing force is measured.	Reference only.
Expansion Force Testing	Measure the pressure required in the balloon to expand the stent to the nominal diameter. The diameter is recorded at three locations at each one atmosphere increment in a saline solution at 37°C.	The expansion pressures need to fall within a range of 2 to 4 atmospheres.
Deployment Testing	Measure the accuracy and repeatability of balloon deployment of the stents.	The deployed stent must be centered within the target area of the simulated iliac artery within the allowable tolerances.
Balloon Inflation/Deflation and Withdraw	Measure the inflation/deflation times of the balloon and verify that balloon can be withdrawn from expanded stent without deforming the stent.	The inflation/deflation time needs to be less than 15 seconds and there is to be no occurrences of the balloon getting caught on the stent during withdrawal.
Stent Compression Force	Measure the force required to compress the expanded stent by both focal point and biplanar methods.	The compression forces should be within ±30% of the Palmaz P104 and P188.
Multiple Balloon Inflations within Stent	Verify that balloon can be inflated to rated burst pressure and deflated 20 times without balloon rupturing or formation of a pinhole.	No balloon ruptures or pin holes in balloon.
Effects of Balloon Rupture on Stent	Verify that balloon rupture will not have any detrimental effects on the stent.	No cracks, metallurgical defects or other mechanical defects attributable to balloon expansion or balloon rupture.
Balloon Burst Strength Post Stent Expansion	Verify that the balloon burst pressure does not decrease when used to expand a stent.	Stent expansion must not reduce the rated burst pressure below the manufacturer rated burst pressure.
Stent Dimensional Measurements Post Balloon Expansion	Measure the length and diameter of the stent post balloon expansion in an anatomical model and as free expansion.	Diameter: Free expansion must be within 5% of nominal balloon diameter and anatomical method must result in expansion and stent conforming to the inside diameter of the model. Length: In both models, the length must be within 2 mm of nominal stated implant length.
Stent Recoil	Measure the elastic springback in the stent when the pressure is released in the balloon.	The elastic recoil needs to be less than 0.5 mm.
Post Balloon Expansion Stent Inspection	Verify that no cracks and metallurgical or mechanical defects attributable to balloon expansion or rupture are seen on the stent.	No cracks, metallurgical defects or other mechanical defects attributable to balloon expansion or rupture.
Pulsatile Fatigue	Subject the stents to 100 million and 400 million cycles and verify that no cracks and metallurgical or mechanical defects occurred due to fatigue or balloon expansion when viewed under light and scanning electron microscopy.	No cracks, metallurgical defects or other mechanical defects attributable to fatigue testing to 100 and 400 million cycles.
Finite Element Analysis/Goodman Analysis	Determine the stress and strain levels during stent crimping and expansion.	Result in stress and strain levels during stent crimping and expansion of <50% of the ultimate stress and strains allowable for 316L.
Stent Percent Open Area	Determined by measuring the surface area on a 3D stent model.	Measurement determination.

Test	Objective/Method	Acceptance Criteria
Magnetic Resonance Imaging	Determine whether MRI has a detrimental influence on the stainless steel implanted stent.	Demonstrate through literature that stent does not pose unacceptable actions under MRI.
Shelf Life Test	Support 3-year shelf-life.	Product and packaging specifications, quality, functionality and safety requirements were demonstrated after 3 years of storage.

C. Animal Testing

A canine animal study was conducted to evaluate the IntraStent DoubleStrut stent. The purpose of this GLP study was to evaluate the *in vivo* performance of the stent in the canine iliac arteries. Incremental sacrifice intervals were 30, 90 and 180 days on a total of ten (10) canines. Parameters included stent migration, excessive intimal hyperplasia (patency), thrombosis, distal embolization and any other unanticipated adverse effects. The cellular and healing response along with tissue coverage of the stent were evaluated histologically at each sacrifice interval. Patency was assessed by angiography and IVUS. The secondary objective of this pre-clinical study was to evaluate the acute performance of the stent during implantation including stent handling characteristics such as deployment, radiopacity and flexibility. The results showed that stent delivery and deployment procedures were uneventful with good stent apposition and accurate stent delivery. All stents implanted in the iliac arteries appeared widely patent with good apposition and no evidence of stent migration or restenosis. No significant inflammation was present in any of the explants and all luminal surfaces were lined by mature endothelium.

D. Sterility Packaging and Shelf Life Testing

Sterility
The IntraStent DoubleStrut stent is ethylene oxide sterilized per the requirements of ANSI/AAMI/ISO 11135:1994, "Medical devices—Validation and routine control of ethylene oxide sterilization." The validation results demonstrated that the sterilization process achieves a minimum sterility assurance level of 10^{-6}, and that residual levels were within the acceptable ranges for an implant according to ISO 10993-7 and AAMI TIR No. 19. Device and package performance were also assessed after sterilization and found to be within specification.

Shelf Life Tests
A three year shelf life has been substantiated for the IntraStent DoubleStrut stent. Product and packaging specifications, quality, functionality and safety requirements were demonstrated after 3 years of storage.

Packaging Tests
The packaging for the IntraStent DoubleStrut Stent was assessed by pouch seal strength validation testing, transportation testing, and packaging validation

testing. The results demonstrate that the device and package performance were found to be within specification.

X. Summary of Clinical Investigations Involving Human Subjects

A multi-center, randomized controlled study was conducted at 23 investigational sites in the United States. The purpose of this study was to demonstrate that the IntraStent DoubleStrut stent is non-inferior to two control stents--the Schneider Wallstent® and the Cordis Palmaz®. A total of 228 patients were treated in the study—115 patients were randomized to the IntraStent DoubleStrut stent and 113 were randomized to receive the control stents.

This randomized clinical study of the IntraStent DoubleStrut stent was used to provide reasonable assurance of the safety and effectiveness of the IntraStent DoubleStrut stent.

Study Endpoints: The primary efficacy endpoint was death within 30 days or primary patency failure at 9 months. Primary patency failure included any restenosis (≥50%) or TVR. The primary safety endpoint was major complication rate at 30-days. Major complications includes death, stroke, bleeding requiring transfusion, myocardial infarction, embolism or any complication that is procedure related or device related which requires a surgical procedure, interventional procedure or an extended stay. Secondary endpoints included acute angiographic success and major complication rate at 30 days.

Patients Studied: Eligible patients had lesions in the common and external iliac artery of up to 100 mm in length with a documented suboptimal PTA result, and a reference vessel diameter of 5 to 10 mm. Baseline characteristics for the patients are presented in Table 4.

Table 4. Baseline Characteristics

Characteristics	IntraStent DoubleStrut Stent (N=115 patients)	Control Stents (N=113 patients)	Difference [95% CI]	P-Value
Age (yrs), mean±SD (N)	62 ± 10	65 ± 10	-2.5 (-0.106,5.158)	0.06
Number of men	65% (75/115)	64% (72/113)	1.5% (-11.1%,14.1%)	0.81
History of smoking	82% (94/115)	77% (87/113)	4.8% (-5.9%,15.4%)	0.65
History of diabetes mellitus	23% (26/115)	27% (30/113)	-3.9% (-15.2%,7.3%)	0.49
Reference vessel diameter (mm), mean±SD (N)	7.6 ± 1.4 (115)	7.6 ± 1.2 (113)	-0.04 (-0.39,0.31)	0.83
Lesion length (mm), mean±SD (N)	30 ± 18 (115)	29 ± 17 (113)	0.5 (-4.0,5.0)	0.83

Numbers are % (counts/sample size) or Mean ± SD

Methods: Informed consent, baseline demographics and medical history data were collected prior to treatment. Patients eligible for the study underwent a PTA and were randomized following an angiographically documented suboptimal result defined by the presence of an unfavorable lesion morphology such as: a) a documented inadequate angiographic and/or hemodynamic result as defined by a 30% or greater residual stenosis resultant to PTA, lesion recoil or intimal flaps and/or b) flow limiting dissections post PTA longer than the initial lesion length, and/or c) a 5 mm Hg or greater mean transtenotic pressure gradient post PTA. Only one limb could be enrolled in the study. Baseline quantitative angiography was performed pre-procedure, post-PTA, and post-procedure in all patients.

Clinical follow-up visits were conducted at post-intervention, 1, 3, 9 and 12 months post-procedure and yearly thereafter. Patients were recommended to receive aspirin (325 mg/day) for at least 3 months following hospital discharge. Duplex Ultrasound was utilized in all patients to make a determination of restenosis at the 9-month follow-up. If Duplex Ultrasound was nondiagnostic, a confirmatory angiogram was performed to document the amount of restenosis present. If angiogram was not done then patency was determined by non-invasive testing (segmental pressure, Doppler wave recording, etc.) if possible. An independent clinical events committee adjudicated all of the major vascular adverse events and deaths. Computer assisted quantitative angiographic analysis (QA), Duplex Ultrasound, non-invasive Doppler wave recording or pulse volume recording, and angiographic measurements were analyzed at independent central laboratories and primary endpoint determination was based on these results.

Results: Follow-up compliance through 9 months was 91.3% (105/115) vs. 89.4% (101/113) in the treatment vs. control groups, respectively; of the returning patients. Based on analysis of 1) primary patency failure (which includes 9-month restenosis and TVR) or 2) death within 30 days of the procedure, there was no difference between outcomes for patients receiving either the IntraStent DoubleStrut Stent vs. the control stents after suboptimal PTA of a lesion in the iliac artery (10.4% vs. 9.8%, p=0.89). The principal effectiveness and safety results are presented in Table 5 (Evaluable) and Table 6 (Intent-to-Treat). Freedom from target lesion revascularization (TLR) events Kaplan-Meier curve is presented in Figure 2.

Gender bias

A higher percentage of males (65%) than females (35%) were included in the trial, which is reflective of the distribution of the disease in the population. Evaluation of the primary efficacy endpoint and acute procedural success by gender showed no significant difference between groups of either gender. There was a significant difference in the major complication rate (<30 days) by gender. Females had an overall major complication rate (<30 days) of 11.4% versus 2.7% for males (p=0.014).

Table 5. Principal Effectiveness and Safety Results (Evaluable)
All randomized U.S. patients (n=228)

EFFICACY MEASURES	IntraStent DoubleStrut Stent (n=115)	Control Stents (n=113)	Difference [95% CI]	P-Value
Primary Efficacy Endpoint	10.4% (10/96)	9.8% (10/102)	-0.6% [-9.0%, 7.8%]	0.89
9-month restenosis	7.4% (7/95)	6.1% (6/99)	-1.3% [-8.4%, 5.7%]	0.71
Death within 30 days	0.0% (0/112)	0.9% (1/112)	0.9% [-0.8%, 2.6%]	0.31
9-month TVR	4.8% (5/104)	4.0% (4/100)	-0.8% [-6.4%, 4.8%]	0.79
Acute Procedural Success	94.6% (105/111)	89.2% (99/111)	-5.4% [-12.6%,1.7%]	0.14
Primary Patency to 9 Months	90.6% (87/96)	92.0% (92/100)	1.4% [-6.5%, 9.3%]	0.73
Bypass within 9 Months	1.8% (2/112)	0% (0/112)	-1.8% [-4.2%, 0.7%]	0.16
TLR-free at 9 Months**	98.2% [95.7%, 100.0%]	99.1% [97.3%, 100.0%]	1.96 [0.18, 21.65]	--
SAFETY MEASURES				
Major Complications ≤ 30 days	2.7% (3/113)	8.9% (10/112)	6.3% [0.2%, 12.3%]	0.04
MAIE ≤ 30 days	0.0% (0/113)	2.7% (3/112)	2.7% [-0.3%, 5.7%]	0.08
Combined MAIE to 9 Months	4.7% (5/106)	4.9% (5/102)	0.2% [-5.6%, 6.0%]	0.95
Stent thrombosis	0.0% (0/106)	2.0% (2/102)	2.0% [-0.7%, 4.7%]	0.16
Major bleeding complications	1.9% (2/106)	4.9% (5/102)	3.0% [-1.9%, 7.9%]	0.23
Major vascular complications	0.9% (1/106)	2.0% (2/102)	1.0% [-2.2%, 4.3%]	0.54
Stroke	0.9% (1/106)	0.0% (0/102)	-0.9% [-2.8%, 0.9%]	0.32
MI	0.0% (0/106)	1.0% (1/102)	1.0% [-0.9%, 2.9%]	0.32

** Kaplan-Meier survival analysis, percent and confidence intervals followed by relative-risk with associated confidence interval from Cox proportional hazards regression.
Numbers are % (counts/sample size)
Difference = Control – Treatment; SE=sqrt(p1*q1/n1+p2*q2/n2) CI=Diff±1.96*SE
Primary Efficacy Endpoint = 1) primary patency failure at 9 months that includes restenosis (≥50%) or TVR or 2) peri-procedural (30 days) death
Acute Procedural Success = Patients with <30% stenosis immediately after the procedure and no major complications during the procedure
MAIE = death to 30 days, in-hospital MI, TVR or amputation
Primary patency = uninterrupted patency of the limb with no procedure performed on or at the margins of the treated segment
Bypass = reestablishment of flow to distal arteries following bypass of target vessel.
Major Complication = Includes death, stroke, bleeding requiring transfusion, myocardial infarction, embolism, or any complication that is procedure or device related which requires a surgical procedure, interventional procedure or extended hospital stay.

Table 6. Principal Effectiveness and Safety Results (Intent-to-Treat)
All randomized U.S. patients (n=228)

EFFICACY MEASURES	IntraStent DoubleStrut Stent (n=115)	Control Stents (n=113)	Difference [95% CI]	P-Value
Primary Efficacy Endpoint	8.7% (10/115)	8.8% (10/113)	0.2% [-7.2%, 7.5%]	0.97
9-month restenosis	6.1% (7/115)	5.3% (6/113)	-0.8% [-6.8%, 52%]	0.80
Death within 30 days	0.0% (0/115)	0.9% (1/113)	0.9% [-.8%, 2.6%]	0.31
9-month TVR	4.3% (5/115)	3.5% (4/113)	-0.8% [-5.9%, 4.2%]	0.75
Acute Procedural Success	91.3% (105/115)	87.6% (99/113)	-3.7% [-11.7%,4.3%]	0.37
Primary Patency to 9 Months	75.7% (87/115)	81.4% (92/113)	5.8% [-4.9%, 16.4%]	0.29
Bypass within 9 Months	1.7% (2/115)	0% (0/113)	-1.7% [-4.1%, 0.7%]	0.16
TLR-free at 9 Months**	98.2% [95.7%, 100.0%]	99.1% [97.3%, 100.0%]	1.96 [0.18, 21.65]	--
SAFETY MEASURES				
Major Complications ≤ 30 days	2.6% (3/115)	8.8% (10/113)	6.2% [0.3%, 12.2%]	0.04
MAIE ≤ 30 days	0.0% (0/115)	2.7% (3/113)	2.7% [-0.3%, 5.6%]	0.08
Combined MAIE to 9 Months	4.3% (5/115)	4.4% (5/113)	0.1% [-5.2%, 5.4%]	0.98

Stent thrombosis	0.0% (0/115)	1.8% (2/113)	1.8% [-0.7%, 4.2%]	0.15
Major bleeding complications	1.7% (2/115)	4.4% (5/113)	2.7% [-1.8%, 7.2%]	0.24
Major vascular complications	0.9% (1/115)	1.8% (2/113)	0.9% [-2.1%, 3.9%]	0.55
Stroke	0.9% (1/115)	0.0% (0/113)	-0.9% [-2.6%, 0.8%]	0.32
MI	0.0% (0/115)	0.9% (1/113)	0.9% [-0.8%, 2.6%]	0.31

** Kaplan-Meier survival analysis, percent and confidence intervals followed by relative-risk with associated confidence interval from Cox proportional hazards regression.

Numbers are % (counts/sample size)

Difference = Control – Treatment; SE=sqrt(p1*q1/n1+p2*q2/n2) CI=Diff±1.96*SE

Primary Efficacy Endpoint = 1) primary patency failure at 9 months that includes restenosis (≥50%) or TVR or 2) peri-procedural (30 days) death

Acute Procedural Success = Patients with <30% stenosis immediately after the procedure and no major complications during the procedure

MAIE = death to 30 days, in-hospital MI, TVR or amputation

Primary patency = uninterrupted patency of the limb with no procedure performed on or at the margins of the treated segment

Bypass = reestablishment of flow to distal arteries following bypass of target vessel.

Major Complication = Includes death, stroke, bleeding requiring transfusion, myocardial infarction, embolism, or any complication that is procedure or device related which requires a surgical procedure, interventional procedure or extended hospital stay.

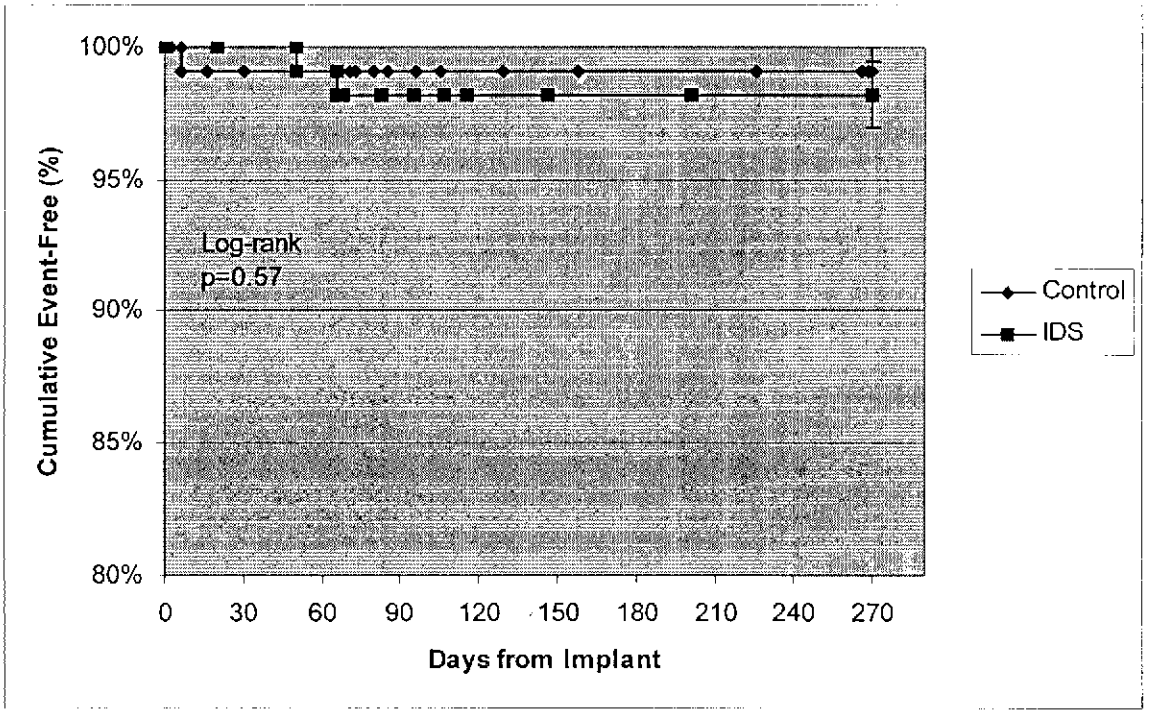

Figure 2. Survival Free From Target Lesion Revascularization to 9 months (Event-Free Survival ±1.5 SE)

All Randomized Patients Treated With Survival Information (N=228)

	30 Day		90 Day		270 Day	
	IDS	**Control**	**IDS**	**Control**	**IDS**	**Control**
Number at risk	111	109	107	104	102	97
Cumulative number with event	0	1	2	1	2	1
Kaplan-Meier Estimate	100%	99.1%	98.2%	99.1%	98.2%	99.1%
Standard Error	N/A	0.009	0.013	0.009	0.013	0.009

XI. Conclusions Drawn from the Studies

The pre-clinical studies indicate that the IntraStent DoubleStrut Stent meet or exceed safety and performance specifications.

Multicenter clinical data found that the rates of major adverse events were similar in the test group treated with the IntraStent DoubleStrut Stent and the control patients treated with the Schneider WALLSTENT® prosthesis and the Cordis Palmaz® stent. There were no significant safety concerns in either treatment group. The early and late effectiveness measures were similar in the test and control groups.

Prior indications for use of stents currently being considered for market approval for use in the iliac artery have been limited to provisional stenting. Because of the high success with iliac stenting, stenting of the iliac artery stenoses or occlusions has become the standard clinical practice regardless of whether the initial PTA was suboptimal. The literature suggests that stenting after suboptimal PTA represents the worst case for testing of a new stent.

The results of the pre-clinical studies and the clinical investigation provide valid scientific evidence and reasonable assurance that the IntraStent DoubleStrut Stent is safe and effective for its intended use.

XII. Panel Recommendation

In accordance with provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH Decision

FDA issued an approval order on June 8, 2004.
The applicant's manufacturing facilities were inspected and found to be incompliance with the Quality System Regulation (21 CFR 820).

XIV. Approval Specifications

Instructions for Use: See labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.